Endovascular repair of an internal mammary artery aneurysm in a patient with Loeys-Dietz syndrome

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Loeys-Dietz syndrome is a condition that predisposes the development of central and peripheral arterial aneurysms and dissections. The standard approach for treatment of these lesions has been open repair. We present the case of a 34-year-old woman with a previous history of multiple open aortic repairs who presented with a right large internal mammary artery aneurysm. The patient was successfully treated with endovascular coil embolization. This case report demonstrates the feasibility of using endovascular interventions to treat unusual aneurysms in patients with Loeys-Dietz syndrome. (J Vasc Surg 2012;55:837-40.)

The underlying genetic lesion in Loeys-Dietz syndrome (LDS) predisposes patients to central as well as peripheral aneurysms. True aneurysms of the internal mammary artery are exceedingly rare. We describe the case of woman with LDS and a large internal mammary artery (IMA) aneurysm with associated consumptive coagulopathy. This was successfully treated with coil embolization with both sac shrinkage and correction of coagulopathy observed in follow up. Follow-up imaging up to 2 years has shown successful thrombosis.

CASE REPORT

The patient is a 34-year-old woman with a history of multiple interventions for vascular anomalies secondary to LDS. In June of 2008, she underwent open repair of the ascending and transverse aortic arch aorta for treatment of an acute type A aortic dissection. In January 2009, a second stage open thoracoabdominal aortic aneurysm repair using multiple side braches for the mesenteric vessels was performed.

A postoperative computed tomography (CT) scan in February 2009 demonstrated stable aneurysmal dilatation of the left subclavian artery, a 1.3-cm aneurysm of the right distal internal mammary artery, and the left common iliac arteries. A repeat CT scan in August 2009 showed development of a 4.0-cm right proximal IMA aneurysm with mural thrombus (Fig 1). While the patient was clinically asymptomatic from this aneurysm, the patient was noted to have coagulation abnormalities consisting of hypofibrinonemia, thrombocytopenia, and hyperfibrinolysis. A hematology consultation was obtained, and a diagnosis of consumptive coagulopathy secondary to the IMA aneurysm was made. The patient was concurrently being evaluated for surgical repair of an incisional hernia. Due to her previous open aortic repairs, the patient was not an ideal candidate for redo-open repair. After discussion with the patient and all the specialists involved, the decision was made to proceed with diagnostic arteriogram and possible coil embolization of the IMA aneurysm.

A diagnostic angiogram using a right common femoral artery approach demonstrated a tortuous aorta, a proximal right subclavian artery dissection, and a right internal mammary artery aneurysm (Fig 2). Retrograde cannulation of the aneurysm sac was performed through an open right brachial artery exposure (Fig 3). A second smaller distal IMA aneurysm was visualized. Attempts to cannulate the distal IMA aneurysm were unsuccessful. As a result, embolization of the larger proximal IMA aneurysm was planned. From the brachial approach, coil embolization was performed using six 12 mm × 14 mm Nester Coils (Cook Medical, Bloomington, IN). Additionally, two 12 mm Amplatzer plugs (AGA Medical Corporation, Plymouth, MN) were placed at the neck of the aneurysm and the proximal right IMA. A completion arteriogram demonstrated absence of filling in the coiled aneurysmal sac (Fig 4).

There were no peri-operative complications, and the patient was discharged home on postoperative day 1. Her 1-, 8-, 12-, and 24-month follow-up CT scans have shown successful embolization of the right IMA, and subsequent complete thrombosis of both the proximal and distal aneurysmal sacs. Subsequent coagulation laboratory work has demonstrated return to baseline of fibrinogen and platelet levels in this patient. Due to the paucity of information on vascular malformations of LDS, the patient is being followed with CT scans every 6 months. Further vascular malformations have necessitated the patient being seen by neurosurgery for bilateral ophthalmic artery aneurysms, for which she has undergone clipping of the right ophthalmic artery aneurysm. She is currently in good health, awaiting planned clipping of the left ophthalmic artery aneurysm.

DISCUSSION

LDS was first described by Loeys et al in 2005 as a autosomal dominant inherited connective tissue disorder due to genetic mutations in either type 1 or type 2 transforming growth factor beta (TGF-β) receptors.[1,2] The hallmarks of this syndrome are the early manifestation of thoracic and abdominal aneurysms, particularly of the aorta, in addition to a marked generalized arterial tortuosity. In a subsequent paper,[2] Loeys et al outlined two separate types: Type 1 presents with craniofacial abnormal-

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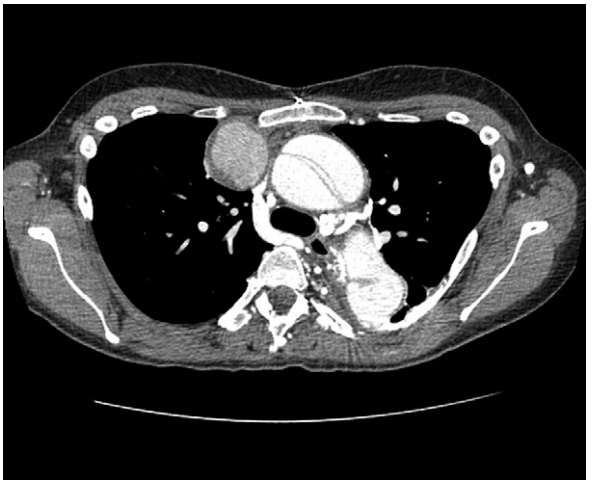

Fig 1. Axial CT scan demonstrating 4 cm right internal mammary artery aneurysm.

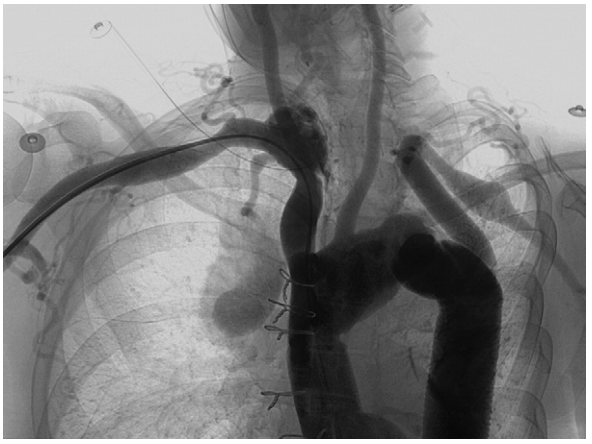

Fig 2. Angiogram demonstrating tortuous aorta, subclavian artery dissection, and right internal mammary aneurysm.

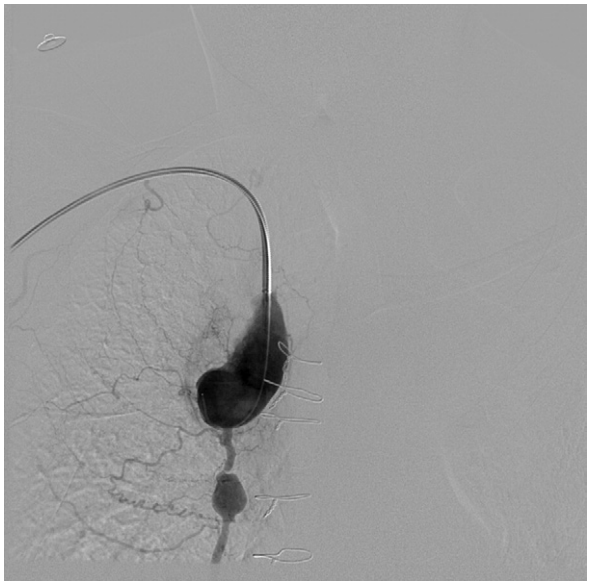

Fig 3. Selective cannulation of right internal mammary artery aneurysm.

Fig 4. Arteriogram postembolization demonstrating occlusion of proximal neck and embolization of aneurysmal sac.

ities (bifid uvula/cleft palate, and orbital hypertelorism) in addition to the previously mentioned vascular abnormalities. Type 2, in contrast, is associated with cutaneous signs (widespread atrophic scars, translucent skin, and easy bruising), joint laxity, and visceral organ rupture, in an absence of the craniofacial abnormalities of type 1.

In the largest cohort to date,[2] 90 patients from 52 families were followed. Among those followed, a total of 137 aneurysms were identified: the majority of which were aortic in nature (75%, n = 103), with the ascending arch the most common aortic location (55%, n = 76). Of the 34 peripheral aneurysms, thoracic branch arteries were the most common (14%, n = 19), followed by head and neck arteries (9%, n = 7), and abdominal arteries (4%, n = 6). The leading causes of death were acute thoracic aortic dissection (67%, n = 18) and acute abdominal aortic dissection (22%, n = 6). As is common in LDS, these occurred at a young age in the absence of aortic diameter changes typically used to predict these events.[1-3] The mean age of death was 26.0 years (range, 0.5-47 years)[2] due to vascular complications, and the mean age of patients requiring vascular surgical intervention was 19.8 years (range, 1.2-46 years).[2] In contrast to vascular Ehlers-Danlos syndrome (type IV), where surgical complication rates can reach 45%,[4,5] surgical interventions are generally successful in LDS, where complication rates as low as 1.7% have been reported.[2,3]

Making the correct diagnosis is vital, as LDS patients are more amenable to surgery, but also at an increased risk of developing aortic dissection and rupture at aneurysm diameters considered safe in other diseases.[1-3] Due to the phenotypic overlap, LDS types 1 and 2 may be misdiag-

Table. Previously reported internal mammary artery (*IMA*) aneurysms

Location	*Etiology*	*Presentation*	*Treatment*	*Outcome*
L IMA aneurysm	Marfan syndrome	Incidental finding during axillary aneurysm rupture	Coil embolization	Uneventful recovery
L IMA aneurysm	Marfan syndrome, prior MVC	Incidental finding on CXR	Coil embolization	Uneventful recovery
L IMA aneurysm	Ehlers-Danlos	Hemothorax	Thoracotomy with ligation of L IMA and drainage of hemothorax	Uneventful recovery
L IMA aneurysm	No risk factors	Hemothorax	Embolization with thoracotomy for drainage of hemothorax	Uneventful recovery
R IMA aneurysm	Atherosclerosis	Anterior mediastinal mass	Open ligation and resection	Uneventful recovery
BL IMA aneurysm	Polyarteritis nodosa	Hemoptysis, incidental finding on CT	Thoracotomy with bilateral resection	Uneventful recovery
L IMA aneurysm	Unknown	Incidental finding on CXR	Thoracotomy with ligation of aneurysm	Uneventful recovery

BL, Bilateral; *CT,* computed tomography; *CXR,* chest x-ray; *L,* left; *MVC,* motor vehicle collision; *R,* right.

nosed as Marfan syndrome type 2, Furlong syndrome, or Shpritzen-Goldberg syndrome, as they all belong to a phenotypical spectrum of TGF-β dysfunction,[6,7] and thus care must be made in making the proper diagnosis on the basis of clinical presentations and genetic tests.

It is possible mild cases of LDS type 2 may be misdiagnosed as Ehlers-Danlos syndrome because of the overlapping cutaneous and visceral organ manifestations of each. Thus, in light of a negative biochemical analysis of collagen type III, LDS type 2 should be considered, with testing for TGF-β receptor mutations performed.[1,2]

Similarly, LDS type 1 may be confused for Marfan syndrome type 2. However, in such cases, Marfan syndrome type 2 is not associated with as severe vascular tortuosity and the widespread aneurysms in LDS are typically confined to the aorta.[1,8] Shprintzen-Goldberg syndrome is another TGF-β receptor 2 mutation leading to craniofacial findings suggestive of LDS type 1; however, the vascular pathology is notably absent.[9]

Due to the recent discovery of LDS, and the spectrum of clinical presentations between LDS type 1 and type 2, and other connective tissue diseases such Marfan syndrome type 2, Ehlers-Danlos syndrome, Furlong syndrome, and Shpritzen-Goldberg syndrome, making the correct diagnosis may pose a challenge.

As previously mentioned, there are scant reports of internal mammary artery aneurysms in the medical literature. While pseudoaneurysms are a known complication of trauma secondary from median sternotomy,[10,11] true aneurysms are associated with connective tissue disorders,[12,13] or vasculitis.[14] The Table describes the location, etiology, and treatment decisions of reported true IMA aneurysms in the literature.[12-18]

Our experience in treating this patient mirrored approaches reported elsewhere for arterial aneurysms in patients with connective tissue disorders,[13,15,16] suggesting that some of these peripheral aneurysms are amenable to endovascular repair. While controversy exists over the role of endovascular interventions in Marfan syndrome and Ehlers-Danlos syndrome,[18,19] the literature has shown promising results for hybrid interventions in aortic aneurysms and dissections in patients with LDS.[20-22] Marine et al report a glue embolus complication for a peripheral endovascular intervention in LDS with otherwise satisfactory results.[23]

The appropriate selection of interventions remains key, as arterial tortuosity may preclude an endovascular intervention, and proper diagnosis remains essential to avoid selecting inappropriate interventions in patients with connective tissue diseases that may phenotypically mimic more common connective tissue diseases. Our experience with this patient has suggested that endovascular repair can yield excellent results. Follow-up CT studies at 6 month intervals have demonstrated stable embolization and complete proximal and distal aneurysm sac thrombosis up to 2 years. The patient has tolerated additional major surgical interventions in the interim. Endovascular repair can be considered as an option in selected peripheral aneurysms in patients with LDS. This experience demonstrates that endovascular repair of focal peripheral aneurysms is an acceptable alternative to open surgical repair in properly selected patients with LDS. The need for frequent and long-term postoperative surveillance imaging cannot be overemphasized in this challenging patient population.

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